

**CLAIMS**

1. A polypeptide which does not comprise the amino acid sequence as recited in SEQ ID NO:10 but which:
  - (i) comprises the amino acid sequence as recited in SEQ ID NO:2;
  - 5 (ii) comprises a fragment of SEQ ID NO:2 which fragment comprises at least a fragment of SEQ ID NO:8 and wherein the polypeptide has the activity of SEQ ID NO:4 or SEQ ID NO:6 (i) or has an antigenic determinant which is specific to a polypeptide comprising SEQ ID NO:2; or
  - (iii) comprises a functional equivalent of (i) or (ii) which has the activity of SEQ ID 10 NO:4 or SEQ ID NO:6 or has an antigenic determinant which is specific to a polypeptide comprising SEQ ID NO:2.
2. A polypeptide according to claim 1 which:
  - (i) comprises, and optionally consists of, the amino acid sequence as recited in SEQ ID NO:4 or SEQ ID NO:6;
  - 15 (ii) comprises, and optionally consists of, a fragment of SEQ ID NO:4 or SEQ ID NO:6 wherein the fragment comprises SEQ ID NO:8 or SEQ ID NO:2 and the polypeptide has the activity of SEQ ID NO:4 or SEQ ID NO:6 or has an antigenic determinant which is specific to a polypeptide comprising SEQ ID NO:2; or
  - (iii) comprises a functional equivalent of (i) or (ii) which has the activity of SEQ ID 20 NO:4 or SEQ ID NO:6 or has an antigenic determinant which is specific to a polypeptide comprising SEQ ID NO:2 and which functional equivalent preferably comprises SEQ ID NO:8 or SEQ ID NO:2.
3. A polypeptide according to claim 1 or 2 which consists of the amino acid sequence as recited in SEQ ID NO:4 or SEQ ID NO: 6.
- 25 4. A polypeptide which is a functional equivalent according to part (iii) of any of the above claims, characterised in that it has at least 70%, 80% or 90% sequence identity to the amino acid sequence as recited in SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO: 6 or SEQ ID NO:8.
5. A polypeptide which is a fragment or a functional equivalent as recited in claim 1, 2 or 3 30 which comprises a sequence having a degree of sequence identity with the amino acid

sequence recited in SEQ ID NO. 8 of greater than 60%, 70%, 80% 90%, 92%, 95%, 98% or 99%.

6. A polypeptide which is a functional equivalent as recited in any one of claims 1, 2, 3 or 5 which comprises the amino acid sequence as recited in SEQ ID NO.8.
- 5 7. A polypeptide which is a fragment as recited in claims 1, 2 or 5 having an antigenic determinant which is specific to a polypeptide comprising SEQ ID NO:2 which consists of 7 or more amino acid residues from the amino acid sequence recited in SEQ ID NO:2 or SEQ ID NO:8.
- 10 8. A purified mRNA or cDNA nucleic acid molecule (or a nucleic acid molecule complementary thereto) which encodes (or whose complement encodes) a polypeptide according to any one of the preceding claims.
9. A purified nucleic acid molecule according to claim 8, which comprises the nucleic acid sequence as recited in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, or SEQ ID NO:7, or is a redundant equivalent or fragment thereof.
- 15 10. A purified nucleic acid molecule according to claim 8 which consists of the nucleic acid sequence as recited in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, or SEQ ID NO:7, or is a redundant equivalent or fragment thereof.
11. A purified nucleic acid molecule which hybridizes under high stringency conditions with SEQ ID NO.3 or SEQ ID NO.5 but which does not hybridise under high  
20 stringency conditions to SEQ ID NO.11.
12. A vector comprising a nucleic acid molecule as recited in any one of claims 8 to 11.
13. A host cell transformed with a vector according to claim 12.
14. A ligand which binds specifically to a polypeptide according to any one of claims 1 to 7.
- 25 15. A ligand according to claim 14, which is an antibody.
16. A compound that either increases or decreases the level of expression or activity of a polypeptide according to any one of claims 1 to 7.
17. A compound according to claim 16 that binds to a polypeptide according to any one of claims 1 to 7 without inducing any of the biological effects of the polypeptide.

18. A compound according to claim 17, which is a natural or modified substrate, ligand, enzyme, receptor or structural or functional mimetic.
19. A polypeptide according to any one of claims 1 to 7, a nucleic acid molecule according to any one of claims 8 to 11, a vector according to claim 12, a host cell according to 5 claim 13, a ligand according to claim 14 or claim 15, or a compound according to any one of claims 16 to 18, for use in therapy or diagnosis of disease.
- 10 20. A method of diagnosing a disease in a patient, comprising assessing the level of expression of a natural gene encoding a polypeptide according to any one of claims 1 to 7, or assessing the activity of a polypeptide according to any one of claims 1 to 7, in tissue from said patient and comparing said level of expression or activity to a control level, wherein a level that is different to said control level is indicative of disease.
21. A method according to claim 20 that is carried out in vitro.
22. A method according to claim 20 or claim 21, which comprises the steps of:
  - 15 a) contacting a ligand according to claim 14 or claim 15 with a biological sample under conditions suitable for the formation of a ligand-polypeptide complex; and
  - b) detecting said complex.
23. A method according to claim 20 or claim 21, comprising the steps of:
  - 20 a) contacting a sample of tissue from the patient with a nucleic acid probe under stringent conditions that allow the formation of a hybrid complex between a nucleic acid molecule according to any one of claims 8 to 11 and the probe;
  - b) contacting a control sample with said probe under the same conditions used in step a); and
  - c) detecting the presence of hybrid complexes in said samples; wherein detection of levels of the hybrid complex in the patient sample that differ from levels of the hybrid 25 complex in the control sample is indicative of disease.
24. A method according to claim 20 or claim 21, comprising:
  - a) contacting a sample of nucleic acid from tissue of the patient with a nucleic acid primer under stringent conditions that allow the formation of a hybrid complex between a nucleic acid molecule according to any one of claims 8 to 11 and the primer;

b)contacting a control sample with said primer under the same conditions used in step a); and

c)amplifying the sampled nucleic acid; and

d)detecting the level of amplified nucleic acid from both patient and control samples;  
5 wherein detection of levels of the amplified nucleic acid in the patient sample that differ significantly from levels of the amplified nucleic acid in the control sample is indicative of disease.

25. A method according to claim 20 or claim 21 comprising:

a)obtaining a tissue sample from a patient being tested for disease;

10 b)isolating a nucleic acid molecule according to any one of claims 8 to 11 from said tissue sample; and

c)diagnosing the patient for disease by detecting the presence of a mutation which is associated with disease in the nucleic acid molecule as an indication of the disease.

26. The method of claim 25, further comprising amplifying the nucleic acid molecule to  
15 form an amplified product and detecting the presence or absence of a mutation in the amplified product.

27. The method of claim 25 or claim 26, wherein the presence or absence of the mutation in the patient is detected by contacting said nucleic acid molecule with a nucleic acid probe that hybridises to said nucleic acid molecule under stringent conditions to form a  
20 hybrid double-stranded molecule, the hybrid double-stranded molecule having an unhybridised portion of the nucleic acid probe strand at any portion corresponding to a mutation associated with disease; and detecting the presence or absence of an unhybridised portion of the probe strand as an indication of the presence or absence of a disease-associated mutation.

25 28. A method according to any one of claims 20 to 27, wherein said disease includes, but is not limited to, reproductive disorders, cell proliferative disorders, including neoplasm, melanoma, lung, colorectal, breast, pancreas, head and neck and other solid tumours; stomach cancer, colon cancer, pancreatic cancer, lung cancer, thoracic cancer, and liver cancer; myeloproliferative disorders, such as leukemia, non-Hodgkin lymphoma,  
30 leukopenia, thrombocytopenia, angiogenesis disorder, Kaposi's sarcoma; autoimmune/inflammatory disorders, including allergy, inflammatory bowel disease,

pancreatitis, arthritis, psoriasis, psoriasis vulgaris, respiratory tract inflammation, asthma, and organ transplant rejection; cardiovascular disorders, including hypertension, oedema, angina, atherosclerosis, thrombosis, sepsis, shock, reperfusion injury, and ischemia, particularly ischemic heart disease; neurological disorders including central nervous system disease, Alzheimer's disease, brain injury, Parkinson's disease, amyotrophic lateral sclerosis, and pain; developmental disorders; metabolic disorders including diabetes mellitus, osteoporosis, and obesity, AIDS, renal disease, particularly idiopathic nephrotic syndrome; disorders related to fibrinolysis; neutrophilic functional disorders (e.g. lazy-leukocyte (chemotaxis-deficient leukocyte) syndrome); inflammatory diseases; wound healing disorders; lung injury; infections including viral infection, bacterial infection, fungal infection and parasitic infection and other pathological conditions..

29. A method according to any one of claims 20 to 27, wherein said disease is a disease in which midkines are implicated.
- 15 30. Use of a polypeptide according to any one of claims 1 to 7 as a growth factor or as a modulator of growth factor activity.
31. A pharmaceutical composition comprising a polypeptide according to any one of claims 1 to 7, a nucleic acid molecule according to any one of claims 8 to 11, a vector according to claim 12, a host cell according to claim 13, a ligand according to claim 14
- 20 32. A vaccine composition comprising a polypeptide according to any one of claims 1 to 7 or a nucleic acid molecule according to any one of claims 8 to 11.
33. A polypeptide according to any one of claims 1 to 7, a nucleic acid molecule according to any one of claims 8 to 11, a vector according to claim 12, a host cell according to claim 13, a ligand according to claim 14 or claim 15, a compound according to any one of claims 16 to 18, or a pharmaceutical composition according to claim 31, for use in the manufacture of a medicament for the treatment of reproductive disorders, cell proliferative disorders, including neoplasm, melanoma, lung, colorectal, breast, pancreas, head and neck and other solid tumours; stomach cancer, colon cancer, pancreatic cancer, lung cancer, thoracic cancer, and liver cancer; myeloproliferative disorders, such as leukemia, non-Hodgkin lymphoma, leukopenia, thrombocytopenia, angiogenesis disorder, Kaposi's sarcoma; autoimmune/inflammatory disorders,

including allergy, inflammatory bowel disease, pancreatitis, arthritis, psoriasis, psoriasis vulgaris, respiratory tract inflammation, asthma, and organ transplant rejection; cardiovascular disorders, including hypertension, oedema, angina, atherosclerosis, thrombosis, sepsis, shock, reperfusion injury, and ischemia, particularly ischemic heart disease; neurological disorders including central nervous system disease, Alzheimer's disease, brain injury, Parkinson's disease, amyotrophic lateral sclerosis, and pain; developmental disorders; metabolic disorders including diabetes mellitus, osteoporosis, and obesity, AIDS, renal disease, particularly idiopathic nephrotic syndrome; disorders related to fibrinolysis; neutrophilic functional disorders (e.g. lazy-leukocyte (chemotaxis-deficient leukocyte) syndrome); inflammatory diseases; wound healing disorders; lung injury; infections including viral infection, bacterial infection, fungal infection and parasitic infection and other pathological conditions.

34. A polypeptide according to any one of claims 1 to 7, a nucleic acid molecule according to any one of claims 8 to 11, a vector according to claim 12, a host cell according to claim 13, a ligand according to claim 14 or claim 15, a compound according to any one of claims 16 to 18, or a pharmaceutical composition according to claim 31, for use in the manufacture of a medicament for the treatment of a disease in which midkine proteins are implicated.
35. A method of treating a disease in a patient, comprising administering to the patient a polypeptide according to any one of claims 1 to 7, a nucleic acid molecule according to any one of claims 8 to 11, a vector according to claim 12, a host cell according to claim 13, a ligand according to claim 14 or claim 15, a compound according to any one of claims 16 to 18, or a pharmaceutical composition according to claim 31.
36. A method according to claim 35, wherein, for diseases in which the expression of the natural gene or the activity of the polypeptide is lower in a diseased patient when compared to the level of expression or activity in a healthy patient, the polypeptide, nucleic acid molecule, vector, ligand, compound or composition administered to the patient is an agonist.
37. A method according to claim 35, wherein, for diseases in which the expression of the natural gene or activity of the polypeptide is higher in a diseased patient when compared to the level of expression or activity in a healthy patient, the polypeptide,

nucleic acid molecule, vector, ligand, compound or composition administered to the patient is an antagonist.

38. A method of monitoring the therapeutic treatment of disease in a patient, comprising monitoring over a period of time the level of expression or activity of a polypeptide according to any one of claims 1 to 7, or the level of expression of a nucleic acid molecule according to any one of claims 8 to 11 in tissue from said patient, wherein altering said level of expression or activity over the period of time towards a control level is indicative of regression of said disease.  
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39. A method for the identification of a compound that is effective in the treatment and/or diagnosis of disease, comprising contacting a polypeptide according to any one of claims 1 to 7 or a nucleic acid molecule according to any one of claims 8 to 11 with one or more compounds suspected of possessing binding affinity for said polypeptide or nucleic acid molecule, and selecting a compound that binds specifically to said nucleic acid molecule or polypeptide.  
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40. A kit useful for diagnosing disease comprising a first container containing a nucleic acid probe that hybridises under stringent conditions with a nucleic acid molecule according to any one of claims 8 to 11; a second container containing primers useful for amplifying said nucleic acid molecule; and instructions for using the probe and primers for facilitating the diagnosis of disease.  
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41. The kit of claim 40, further comprising a third container holding an agent for digesting unhybridised RNA.  
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42. A kit comprising an array of nucleic acid molecules, at least one of which is a nucleic acid molecule according to any one of claims 8 to 11.
43. A kit comprising one or more antibodies that bind to a polypeptide as recited in any one of claims 1 to 7; and a reagent useful for the detection of a binding reaction between said antibody and said polypeptide.  
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44. A transgenic or knockout non-human animal that has been transformed to express higher, lower or absent levels of a polypeptide according to any one of claims 1 to 7.
45. A method for screening for a compound effective to treat disease, by contacting a non-human transgenic animal according to claim 44 with a candidate compound and determining the effect of the compound on the disease of the animal.  
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